

REMARKS

The purpose of this Preliminary Amendment is to eliminate multiple dependent claims in order to avoid the additional fee. Applicants reserve the right to reintroduce claims to canceled combined subject matter.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version With Markings to Show Changes Made**".

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) A compound according to claim 1 ~~or 2~~ having the formula 2(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl) acetamide ([¹⁸F]-EF2).
4. (Amended) A compound according to claim 1 ~~or 2~~ having the formula 2(2-nitro-1H-imidazol-1-yl)-N-(2,2,3,3,3-pentafluoropropyl) acetamide ([¹⁸F]-EF5).
5. (Amended) A method for the synthesis of a compound according to ~~one of the~~ claims 1-4, comprising the step of coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F]-labelled perfluoroalkyl amine derivative.
7. (Amended) A method for the synthesis of a compound according to ~~of one of the~~ claims 1-4 or the corresponding non-labelled form thereof, comprising the steps of:
 - a) adding a THF solution of 2 of Figure 7 to a suspension of PYBOP in THF followed by Et₃N,
 - b) adding an amine 1 of Figure 7 and Et₃N to the solution obtained in step (a),
 - c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,
 - d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,
 - e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,
 - f) purifying the residue obtained after step (e) by column chromatography on silica gel,
 - g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,
 - h) reacting said persulphurated derivative obtained from step (g) with a suitable labelled or non-labelled perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluor atom incorporation,
 - i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and
 - j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the [¹⁸F]-labelled or non-labelled perfluorinated-nitroaromatic compound.

9. (Amended) A [^{18}F]-labelled compound obtainable by a method according to ~~one of the~~ claims 5, 6, 7 or 8.
12. (Amended) A first intermediate compound according to claim 10 ~~or 11~~, obtainable via steps a to g of the ~~—the method as claimed in claim 7 of the invention.~~
13. (Amended) A first intermediate compound according to claim 10, ~~11 or 12~~, being ethyl 3-(N-phthalimido)-aminopropanedithioate, N-3,3,3-trifluoro-2-thioxopropyl phthalimide, N-{[2-(trifluoromethyl)-1, 3-dithiolan-2-yl] methyl} phthalimide, methyl(or ethyl) 3-phthalimide-2,2-difluoropropanedithioate, N-[2,2-difluoro-3,3,3-tris(methylthio) propyl] phthalimide or N-[2,2-difluoro-3,3,3-tris(ethylthio)propyl] phthalimide.
- ~~16.~~ (Amended) A second intermediate compound according to claim 14, ~~15 or 16~~ obtainable via steps a to h of the method of the invention.
17. (Amended) A second intermediate compound according to claim 14, being N-(3,3,3-trifluoropropyl)phthalimide.
20. (Amended) A third intermediate [^{18}F]-labelled compound obtainable via steps a to i of the ~~method as claimed in claim 7 or 8 of the invention.~~
21. (Amended) Use of compound according to ~~one of the~~ claims 1-4 as bioactive compound.
22. (Amended) A [^{18}F] labelled bioactive compound synthesized using as intermediates a first ~~intermediate as claimed in one of the claims 10-13~~, a second intermediate ~~as claimed in one of the claims 14-17~~ and a third intermediate as claimed in ~~one of the claims 10-13~~.

23. (Amended) A [^{18}F] labeled bioactive compound synthesized using as intermediates a first intermediate as claimed in ~~one of the claims 1-13~~ 10.
24. (Amended) Method of perfluorination using as an intermediate a compound as claimed in ~~one of the claims 1-13~~ 10.
26. (Amended) A method for the detection of tissue hypoxia in a patient comprising:
- introducing an [^{18}F] labelled nitroimidazole compound of ~~any of claims 1 to 4~~ into said patient,
 - imaging tissue hypoxia in said patient, and
 - quantifying tissue hypoxia in said patient.
28. (Amended) A method for the detection of tissue hypoxia in a tissue comprising:
- introducing an [^{18}F] labelled nitroimidazole compound of ~~any of claims 1 to 4~~ into a patient,
 - removing a tissue sample from said patient, and
 - analysing the emission in said tissue sample by autoradiography.
29. (Amended) A method for the detection of an [^{18}F] labelled bioactive compound in a patient comprising:
- introducing an [^{18}F] labelled bioactive compound according to claim ~~1-4~~ into said patient,
 - imaging the presence of said [^{18}F] labelled bioactive compound in said patient, and
 - optionally, quantifying the presence of said [^{18}F] labelled bioactive compound in said patient.
30. (Amended) A method for the detection of [^{18}F] labelled bioactive compound in a tissue comprising:
- introducing an [^{18}F] labelled bioactive compound of claim ~~1-4~~ into a patient,
 - taking a tissue sample from said patient, and
 - analysing the emission in said tissue sample by autoradiography.